

WE CLAIM:

1       1. An electrode comprising:  
2              a non-corroding, conducting wire coated with  
3              an insulating polymer;  
4              a recess at one end of said coated wire,  
5              forming a channel in the insulating polymer coat devoid  
6              of wire and bounded at one end by the wire and at an  
7              opposite end by the environment adjacent the coated  
8              wire;  
9              a multilayered polymeric composition within  
10     said channel, the composition comprising:  
11              a redox layer adjacent to and contacting  
12     said wire, the redox layer comprising a redox enzyme  
13              crosslinked to a redox polymer;  
14              a biocompatible polymer layer adjacent to the  
15     environment outside the coated wire; and  
16              an analyte diffusion limiting barrier layer  
17     positioned between said redox layer and said  
18     biocompatible layer.

1       2. A method for producing an in vivo glucose  
2     biosensor comprising the steps of:  
3              coating a non-corroding metal or carbon wire  
4     with a biocompatible insulating polymer containing less  
5     than 5% water when in equilibrium with physiological  
6     body fluids to form a coated wire;  
7              etching said coated wire to form a recess at  
8     one end of said coated wire, said recess devoid of  
9     metal or carbon;  
10          immobilizing within said recess, adjacent to  
11     said wire, a redox composition comprising glucose  
12     oxidase and a redox polymer;

13 evercoating contents of the recess with a  
14 biocompatible polymer;  
15 wherein said etched wire with said polymer  
16 overcoated recess and contents form a glucose biosensor  
17 having substantially no current output at zero glucose  
18 concentration, even in the presence of interfering  
19 electroreactive species.

1       3. A method for measuring glucose  
2 concentration in an animal comprising the steps of:  
3       implanting subcutaneously in an animal the  
4 electrode of claim 1;  
5       placing a second reference counter or  
6 combined reference and counter electrode on or in the  
7 skin of the animal;  
8       connecting the electrodes through an  
9 electrical circuit; and  
10      obtaining readings to measure glucose  
11 concentration.

1       4. The method of claim 3, wherein at least  
2 two electrodes of claim 1 are implanted subcutaneously  
3 in said animal, and wherein paired readings of said two  
4 electrodes that do not differ more than two standard  
5 deviations are accepted as correctly measuring the  
6 concentration of glucose.

1       5. A biosensor comprising:  
2       a non-corroding metal or carbon electrode;  
3       a sensing layer adjacent to and in electrical  
4 contact with the electrode, the sensing layer  
5 comprising a redox polymer and a redox enzyme;

6           a biocompatible layer coating an outer  
7    surface of the electrode and sensing layer and adjacent  
8    to an environment outside the sensor, said  
9    biocompatible layer comprised of a biocompatible  
10   polymer containing not less than 20% water by weight  
11   when in equilibrium with physiological body fluids.

1         6. The biosensor of claim 5, wherein said  
2    electrode is part of an electrically conducting wire.

1         7. The biosensor of claim 1, wherein said wire is  
2    coated along its length, but not at its tip, with an  
3    electrically insulating polymer containing less than 5%  
4    water by weight when in equilibrium with physiological  
5    body fluids.

1         8. The biosensor of claim 7, wherein said tip of  
2    the wire is recessed in the insulating polymer coat,  
3    forming a recessed channel having a length from tip of  
4    the sensor to the recessed wire of between  
5    approximately 20  $\mu\text{m}$  and 1 mm.

1         9. The biosensor of claim 8, wherein said redox  
2    polymer is derived from poly(1-vinylimidazole) or a  
3    copolymer of (1-vinyl imidazole) bound to a metal ion  
4    selected from the group consisting of  $\text{Os}^{3+/2+}$ ,  $\text{Ru}^{3+/2+}$ , and  
5     $\text{Fe}^{3+/2+}$ .

1         10. The biosensor of claim 1, wherein the redox  
2    potential of said redox polymer is not more reducing  
3    than about -0.15V and not more oxidizing than about  
4    +0.15V versus the standard calomel electrode in an  
5    aqueous solution at about pH 7.4.

1        11. The biosensor of claim 1 further comprising  
2        an interference eliminating layer comprising a  
3        peroxidase enzyme.

1        12. The biosensor of claim 1, wherein said redox  
2        enzyme catalyzes the oxidation of glucose.

1        13. The biosensor of claim 12, wherein said redox  
2        enzyme is glucose oxidase.

1        14. The biosensor of claim 13, wherein said redox  
2        enzyme is recombinant glucose oxidase.

1        15. The biosensor of claim 1, wherein said redox  
2        enzyme catalyzes the oxidation of lactate.

1        16. The biosensor of claim 11, wherein said  
2        interference eliminating layer further comprises an  
3        enzyme which catalyzes a hydrogen peroxide-generating  
4        reaction.

1        17. The biosensor of claim 7, wherein said  
2        insulating polymer is selected from the group  
3        consisting of polyimide, polyester, polyurethane, and  
4        perfluoroinated polymer.

1        18. The biosensor of claim 1, further comprising  
2        a glucose flux limiting layer positioned between said  
3        sensing layer and said biocompatible layer, the glucose  
4        flux limiting layer comprising a polyanionic,  
5        polycationic, or zwitterionic polymer.

1        19. The biosensor of claim 1 wherein the outside  
2 diameter of the insulated wire is less than about  
3 0.3mm.

1        20. The biosensor of claim 1 wherein the redox  
2 enzyme and redox polymer are crosslinked.

1        21. A method for manufacturing the biosensor of  
2 claim 6, comprising the steps of:

3        electrically charging droplets of an aqueous  
4 polymer;

5        applying a potential to the electrode such that  
6 the electrically charged droplets are attracted to said  
7 electrode; and

8        applying the charged droplets of polymer to the  
9 electrode to form a polymer coated electrode.

1        22. The method of claim 21, wherein the  
2 electrically charged droplets are applied to a non-  
3 insulated tip of an electrically insulated wire.

1        23. A method for manufacturing the biosensor of  
2 claim 1, wherein said recessed channel is formed by  
3 electrolytic dissolution of part of the electrically  
4 conducting wire, with an oxidizing electrical potential  
5 of not less than 0.3 volts versus the standard calomel  
6 electrode being maintained on the dissolving wire, said  
7 wire being immersed in an aqueous solution containing  
8 at least one anion selected from the group consisting  
9 of CN<sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup>, and I<sup>-</sup> at a concentration of at least  
10 approximately 0.1M.

1        24. A method for measuring the concentration of a  
2 biochemical in an animal comprising:

3           contacting body fluid of an animal the electrode  
4 of claim 1; and

5           determining from the electrical signal generated  
6 at the electrode the concentration of biochemical in  
7 the body fluid.

1           25. The method of claim 25, wherein said  
2 contacting is implanting the electrode subcutaneously.

1           26. The method of claim 25, wherein said  
2 subcutaneous tissue is blood.

1           27. The method of claim 24, wherein said  
2 biochemical is glucose.

1           28. The method of claim 24, wherein said  
2 biochemical is lactate.

1           29. The method of claim 24, wherein at least two  
2 electrodes are simultaneously implanted and wherein  
3 their readings are compared and accepted as valid only  
4 when they do not differ by more than two standard  
5 deviations, the standard deviations being calculated  
6 from paired measurements with a pair of implanted  
7 electrodes.

1           30. A method for calibrating the implanted  
2 electrode of claim 1, comprising the steps of:

3           analyzing the concentration of the analyte to be  
4 measured by the electrode of claim 8 in one or more  
5 samples of fluid withdrawn from a patient, where the  
6 concentration of the chemical does not change  
7 substantially in the withdrawn samples;

8 relating the current generated by the electrode at  
9 the time the sample is withdrawn to the concentration  
10 of biochemical.

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